



91556-00003

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Santosh R. D'Mello, et al.

Serial No.: 10/688,759

Filing Date: October 17, 2003

For: The Use of C-Raf
Inhibitors for the Treatment
of Neurodegenerative
Diseases

CERTIFICATE OF MAILING	
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on:	
<u>January 4, 2004</u>	(Date of Mailing)
<u>Janice Schigut</u>	(Name of Person Mailing Document)
<u>Janice Schigut</u>	(Signature)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INFORMATION DISCLOSURE STATEMENT

Pursuant to the duty of disclosure under 37 C.F.R. §1.56, Applicant submits this statement. This submittal is made in accordance with 37 C.F.R. §§1.97 and 1.98 and §609 of the Manual of Patent Examining Procedure. The patents, publications and other information herein are listed on the attached Form PTO-1449. Copies of the listed references are submitted herewith.

Applicant hereby expressly reserves the right to swear behind the effective dates of any of the above patents and other publications and to question the relevance and

materiality of the Patents and Publications listed herein, in whole, in part, or in combination, subsequent to filing this Information Disclosure Statement.

It is believed no fee is due for submission of this paper. If this is incorrect, the Commissioner is hereby authorized to charge any fee due to Locke Liddell & Sapp LLP Deposit Account No. 12-1781.

Respectfully submitted,

By: Scott C. Sample
Scott C. Sample
Registration No. 52,189

Date: January 14, 2004

LOCKE LIDDELL & SAPP LLP
2200 Ross Avenue, Ste. 2200
Dallas, TX 75201-6776
(214) 740-8489
(214) 740-8800 (fax)



FORM 98-3

Page 1 of 4

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE
(Rev. 2-32) PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.
91556-00003SERIAL NO.
10/688,759INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(Use several sheets if necessary)

APPLICANT
Santosh R. D'Mello, et al.FILING DATE
October 17, 2003

GROUP

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	1						
	2						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	TRANSLATION YES NO
	1						
	2						

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	1	ALESSI, D.R., et al. (1995) "PD 098059 Is a Specific Inhibitor of the Activation of Mitogen-Activated Protein Kinase Kinase In Vitro and In Vivo", J. Biol Chem. 270, 27489-27494.
	2	ANDERSON, C.N., et al. (1999) "A Role for MAPK/ERK in Sympathetic Neuron Survival: Protection Against a p53-Dependent, JNK-Independent Induction of Apoptosis by Cytosine Arabinoside", J Neurosci. 19, 664-673.
	3	BACCARINI, M. (2002) "An Old Kinase On a New Path: Raf and Apoptosis", Cell Death Differ. 9, 783-785.
	4	BARR, R.K., et al. (2001) "The c-Jun N-Terminal Protein Kinase Family of Mitogen-Activated Protein Kinases (JNK MAPKs)", Int. J. Biochem. Cell Biol. 33, 1047-1063.
	5	BONNI, A., et al. (1999) "Cell Survival Promoted by the Ras-MAPK Signaling Pathway by Transcription-Dependent and Independent Mechanisms", Science 286, 1358-1362.



6	BRUCKNER, S.R., et al. (2001) "JNK3 Contributes to c-Jun Activation and Apoptosis But Not Oxidative Stress in Nerve Growth Factor-Deprived Sympathetic Neurons", J. Neurochem. 78, 298-303.
7	BRUCKNER, S.R., et al. (2002) "JNK3 Contributes to c-jun Induction and Apoptosis in 4-Hydroxynonenal-Treated Sympathetic Neurons", J. Neurosci Res. 70, 665-670.
8	BRUNET, A., et al. (2001) "Transcription-Dependent and Independent Control of Neuronal Survival by the P13K-Akt Signaling Pathway", Curr. Opin. Neurobiol. 11, 297-305.
9	CHANG, L.K., et al. (2002) "Mitochondrial Involvement in the Point of No Return in Neuronal Apoptosis", Biochimie, 84, 223-231.
10	COFFEY, E.T., et al. (2002) "c-Jun N-Terminal Protein Kinase (JNK) 2/3 is Specifically Activated by Stress, Mediating c-Jun Activation, In The Presence of Constitutive JNK1 Activity in Cerebellar Neurons", J. Neurosci. 22, 4335-4345.
11	COPANI, A., et al. (2001) "Activation of Cell-Cycle-Associated Proteins In Neuronal Death: A Mandatory or Dispensable Path?", Trends Neurosci. 24, 25-31.
12	CROWDER, R.J., et al. (1998) "Phosphatidylinositol 3-Kinase and Akt Protein Kinase Are Necessary and Sufficient for the Survival of Nerve Growth Factor-Dependent Sympathetic Neurons", J. Neurosci. 18, 2933-2943.
13	DATTA, S.R., et al. (1997) "Akt Phosphorylation of BAD Couples Survival Signals to the Cell-Intrinsic Death Machinery", Cell 91, 231-241.
14	DESHMUKH, M., et al. (1997) "Programmed Cell Death in Neurons: Focus On the Pathway of Nerve Growth Factor Deprivation-Induced Death of Sympathetic Neurons", Mol. Pharmacol. 51, 897-906.
15	DHILLON A.S., et al. (2002) "Untying the Regulation of the Raf-1 Kinase", Arch Biochem Biophys. 404, 3-9.
16	D'MELLO, S.R., et al. (1993) "Induction of Apoptosis in Cerebellar Granule Neurons by Low Potassium: Inhibition of Death by Insulin-Like Growth Factor I and cAMP", Proc. Natl. Acad. Sci. U S A 90, 10989-10993.
17	D'MELLO, S.R., et al. (1997) "Insulin-Like Growth Factor and Potassium Depolarization Maintain Neuronal Survival by Distinct Pathways: Possible Involvement of PI 3-Kinase in IGF-1 Signaling", J. Neurosci. 17, 1548-1560.
18	D'MELLO, S.R. (1998) "Molecular Regulation of Neuronal Apoptosis", Curr. Top. Dev. Biol. 39:187-213.
19	DUDEK, H., et al. (1997) "Regulation of Neuronal Survival by the Serine-Threonine Protein Kinase Akt.", Science 275, 661-665.
20	DUNCIA, J.V., et al. (1998) "MEK Inhibitors: The Chemistry and Biological Activity of U0126, Its Analogs, and Cyclization Products", Bioorg Med Chem Lett. 8, 2839-2844.
21	EILERS, A., et al. (1998) "Role of the Jun Kinase Pathway in the Regulation of c-Jun Expression and Apoptosis in Sympathetic Neurons", J Neurosci. 18, 1713-1724.
22	ESTUS, S., et al. (1994) "Altered Gene Expression in Neurons During Programmed Cell Death: Identification of c-Jun as Necessary for Neuronal Apoptosis", J Cell Biol. 127, 1717-1727.
23	FAVATA, M.F., et al. (1998) "Identification of a Novel Inhibitor of Mitogen-Activated Protein Kinase Kinase", J Biol Chem. 273, 18623-18632.
24	FOO, S.Y., et al. (1999) "NF- κ B to the Rescue: RELs, Apoptosis and Cellular Transformation", Trends Genet. 15, 229-235.
25	GONZALEZ-POLO, R.A., et al. (2001) "Mechanisms of MPP(+) Incorporation Into Cerebellar Granule Cells", Brain Res Bull. 56, 119-123.
26	HALL-JACKSON, C.A., et al. (1999) "Paradoxical Activation of Raf by a Novel Raf Inhibitor", Chem Biol. 6, 559-568.
27	HAM, J., et al. (1995) A c-Jun Dominant Negative Mutant Protects Sympathetic Neurons Against Programmed Cell Death", Neuron 14, 927-939.
28	HAN, B.H., et al. (2000) "BDNF Protects the Neonatal Brain From Hypoxic-Ischemic Injury In Vivo Via the ERK Pathway", J Neurosci. 20, 5775-5781.
29	HARRIS, C.A., et al. (2002) "Inhibition of the c-Jun N-Terminal Kinase Signaling Pathway by the Mixed Lineage Kinase Inhibitor CEP-1347 (KT7515) Preserves Metalloproteinase and Growth of Trophic Factor-Deprived Neurons", J Neurosci. 22, 103-113.
30	HINDLEY, A., et al. (2002) "Extracellular Signal Regulated Kinase (ERK)/Mitogen Activated Protein Kinase (MAPK)-Independent Functions of Raf Kinases", J Cell Sci. 115, 1575-1581.

31	JANSEN, B., et al. (1999) "Novel Ras Antagonist Blocks Human Melanoma Growth", <i>Proc Natl Acad Sci USA</i> 96, 14019-14024.
32	JUN., et al. (1999) "Tangled Webs: Evidence of Cross-Talk Between C-Raf-1 and Akt", <i>Sci STKE</i> . 13, PE1, 1-4.
33	KOULICH, E., et al. (2001) "NF- κ B Is Involved In the Survival of Cerebellar Granule Neurons: Association of IkappaBbeta Phosphorylation With Cell Survival", <i>J Neurochem</i> . 76, 1188-1198.
34	KUMARI, S., et al. (2001) "Distinct Phosphorylation Patterns Underlie Akt Activation by Different Survival Factors in Neurons", <i>Brain Res Mol Brain Res</i> . 96, 157-162.
35	KUNIMOTO, M. (1994) "Methylmercury Induces Apoptosis of Rat Cerebellar Neurons In Primary Culture", <i>Biochem Biophys Res Commun</i> . 204, 310-317.
36	JOHNSON, E.M., et al. (1993) "Molecular Mechanisms of Developmental Neuronal Death", <i>Annu. Rev. Neurosci.</i> 16, 31-46.
37	LACKEY, K., et al. (2000) "The Discovery of Potent cRaf1 Kinase Inhibitors", <i>Bioorg Med Chem Lett</i> . 10, 223-226.
38	LIN, Y.Z., et al. (1995) "Inhibition of Nuclear Translocation of Transcription Factor NF- κ B By A Synthetic Peptide Containing A Cell Membrane-Permeable Motif and Nuclear Localization Sequence", <i>J Biol Chem</i> . 270, 14255-14258.
39	LIU, D.X., et al. (2001) "Neuronal Apoptosis at the G1/S Cell Cycle Checkpoint", <i>Cell Tissue Res</i> . 305, 217-228.
40	LINSEMAN, D.A., et al. (2002) "Insulin-Like Growth Factor-1 Blocks Bcl-2 Interacting Mediator of Cell Death (Bim) Induction and Intrinsic Death Signaling In Cerebellar Granule Neurons", <i>J Neurosci</i> . 22, 9287-9297.
41	MATTSON, M.P. (2000) "Apoptosis In Neurodegenerative Disorders", <i>Nat Rev Mol Cell Biol</i> . 1, 120-129.
42	MAZZONI, I.E., et al. (1999) "Ras Regulates Sympathetic Neuron Survival by Suppressing the p53-Mediated Cell Death Pathway", <i>J Neurosci</i> . 19, 9716-9727.
43	MILLER, T.M., et al. (1997a) "Inhibition of Phosphatidylinositol 3-Kinase Activity Blocks Depolarization- and Insulin-Like Growth Factor 1-Mediated Survival of Cerebellar Granule Cells", <i>J Biol Chem</i> . 272, 9847-9853.
44	O'HARE, M., et al. (2002) "Cyclin-Dependent Kinases as Potential Targets to Improve Stroke Outcome", <i>Pharmacol Ther</i> . 93, 135-43.
45	OPPENHEIM, R.W. (1991) "Cell Death During Development of the Nervous System", <i>Annu. Rev. Neurosci.</i> 14, 453-501.
46	PADMANABHAN, J., et al. (1999) "Role of Cell Cycle Regulatory Proteins in Cerebellar Granule Neuron Apoptosis", <i>J Neurosci</i> . 19, 8747-8756.
47	PARK, D.S., et al. (1997a) "Cyclin Dependent Kinase Inhibitors and Dominant Negative Cyclin Dependent Kinase 4 and 6 Promote Survival of NGF-Deprived Sympathetic Neurons", <i>J Neurosci</i> . 17, 8975-8983.
48	PARK, D.S., et al. (1997b) "G1/S Cell Cycle Blockers and Inhibitors of Cyclin-Dependent Kinases Suppress Camptothecin-Induced Neuronal Apoptosis", <i>J Neurosci</i> . 17, 1256-1270.
49	PARK, D.S., et al. (1998a) "Cyclin-Dependent Kinases Participate in Death of Neurons Evoked by DNA-Damaging Agents", <i>J Cell Biol</i> . 143, 457-467.
50	PARK, D.S., et al. (1998b) "Multiple Pathways of Neuronal Death Induced by DNA-Damaging Agents, NGF Deprivation, and Oxidative Stress", <i>J. Neurosci</i> . 18, 830-840.
51	PEARSON, G., et al. (2000) "Uncoupling Raf1 From MEK1/2 Impairs Only a Subset of Cellular Responses to Raf Activation", <i>J Biol Chem</i> . 275, 37303-37306.
52	PUTCHA, G.V., et al. (2001) "Induction of BIM, A Proapoptotic BH3-Only BCL-2 Family Member, Is Critical for Neuronal Apoptosis", <i>Neuron</i> 29, 615-628.
53	SAPORITO, M.S., et al. (2002) "Discovery of CEP-1347/KT-7515, An Inhibitor of the JNK/SAPK Pathway for the Treatment of Neurodegenerative Diseases", <i>Prog Med Chem</i> . 40, 23-62.
54	TROTTER, L., et al. (2002) "Mitogen-Activated Protein Kinase Kinase 7 is Activated During Low Potassium-Induced Apoptosis in Rat Cerebellar Granule Neurons", <i>Neurosci Lett</i> . 320, 29-32.
55	VILA, M., et al. (2003) Targeting Programmed Cell Death In Neurodegenerative Diseases", <i>Nat Rev Neurosci</i> . 4, 365-375.
56	VALLALBA, M., et al. (1997) "Pituitary Adenylate Cyclase-Activating Polypeptide (PACAP-38) Protects Cerebellar Granule Neurons From Apoptosis by Activating the Mitogen-Activated Protein Kinase (MAP Kinase) Pathway", <i>J. Neurosci</i> . 17, 83-90.
57	WATSON, A., et al. (1998) "Phosphorylation of c-Jun Is Necessary for Apoptosis Induced by Survival Signal Withdrawal In Cerebellar Granule Neurons", <i>J Neurosci</i> . 18, 751-762.
58	WIESE, S., et al. (2001) "Specific Function of B-Raf in Mediating Survival of Embryonic Motoneurons and Sensory Neurons", <i>Nat Neurosci</i> . 4, 137-142.
59	WEISZ, B., et al. (1999) "A New Functional Ras Antagonist Inhibits Human Pancreatic Tumor Oncogene", 18, 2579-2588.

60		WESTON, C.R., et al. (2002) "The JNK Signal Transduction Pathway", Curr Opin Genet Dev. 12, 14-21.
61		WOLFMAN, J.C., et al. (2002) "Cellular N-Ras Promotes Cell Survival by Downregulation of Jun N-Terminal Protein Kinase and p38", Mol Cell Biol. 22, 1589-1606.
62		XU, Z, et al. (2001) "The MLK Family Mediates c-Jun N- Terminal Kinase Activation in Neuronal Apoptosis", Mol Cell Biol. 21, 4713-4724
63		
64		
65		
66		
66		
67		
68		
69		
70		
71		
72		
73		
74		
75		
76		
77		
78		
79		
80		
81		
82		
83		
84		
85		
86		

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.